PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: McGLYNN, Paul
	: BAKALE, Roger
	: STURGE, Craig
Serial No.	: 10/728,873
Filing Date	: December 8, 2003
For	: LEVALBUTEROL SALT
Art Unit	: 1621
Examiner	: PUTTLITZ, Karl J.
Confirm No.	: 1167
Docket No.	: 00324/US1
Customer No.	: 024330

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

UNITED STATES

Sir:

DECLARATION UNDER 37 C.F.R. 1.132

I, Paul McGlynn, declare that:

I hold the degrees of B.Sc(Hons), Biochemistry from the University of Hull, Hull, United Kingdom (1985), M.Sc. Analytical Chemistry, The Liverpool Polytechnic, Liverpool,

United Kingdom (1988), and Doctor of Philosophy (PhD) in Inorganic Chemistry from UMIST (the University of Manchester Institute of Science and Technology), Manchester, United Kingdom (1992).

I have been employed since 1999 by Sepracor, Inc., in the following capacities:

February 1999 to July, 2001 - Manager of Aerosol Development

July 2001 to January 2003 - Associate Director of Aerosol Development

January 2003 to January 2006 - Director, Aerosol Development

January 2006 to Date - Senior Director, Aerosol Development

I am named as an inventor in this United States patent application and several foreign patent applications and patents.

I further declare that:

1. Experiments were performed by scientists working for Sepracor to measure the solubility of levalbuterol hydrochloride and levalbuterol L-tartrate in ethanol/HFA blends, a carrier system commonly used in aerosol formulations for use in metered dose inhalers. The experiments and results are described on page 19 of the specification for this patent application.

2. Scientists working for Sepracor prepared a large number of different salts of levalbuterol to find out whether or not they formed crystalline salts and if so in what morphology. One of the many salts they prepared was the sulfate, and another was the L-tartrate. It was found that the sulfate afforded crystals of a suitable needle-like form

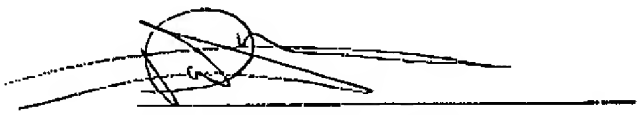
that could be micronised and formulated with a chlorofluorocarbon as the propellant. This chlorofluorocarbon formulation was then used in initial clinical trials. However, it was found that the micronised crystals of the sulfate salt tend to change physical form and aggregate in the presence of humidity. This is highly undesirable in particles intended to be administered to patients using a metered dose inhaler, because consistent dosing cannot be assured. It was concluded that the development of a metered dose inhaler containing the sulfate salt should be discontinued.

The problem with the sulfate crystals can be appreciated by comparing the results of storing micronised levalbuterol sulfate under ambient and controlled humidity conditions. In one series of experiments, a sample of levalbuterol sulfate was micronised then partitioned into two lots. One lot was stored in a glove box at 12% relative humidity for three months, and the other was stored for the same period under ambient conditions. At the start of the experiments, the micronised powder was free flowing and fluffy. At the end of the period, the material stored under controlled humidity conditions was unchanged, whereas that stored under ambient conditions had aggregated. Analysis of the two samples by X-ray powder diffraction showed that the aggregated material had changed crystal form.

From these results, I conclude that the hydrochloride and the sulfate salts of levalbuterol afford particles that possess properties undesirable in a material intended to be administered using a metered dose inhaler.

In contrast, levalbuterol L-tartrate has been found to afford crystalline particles suitable for administration using a metered dose inhaler. The salt has been commercialized and is now sold by Sepracor, Inc under the brand name XOPENEX HFA.

I further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (18 U.S.C. 1001), and may jeopardize the validity of the application or any patent issuing thereon.



Paul McGlynn, PhD.

22nd December 2006

Date

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